

STATE OF MICHIGAN
DEPARTMENT OF INSURANCE AND FINANCIAL SERVICES
Before the Director of Insurance and Financial Services

In the matter of:

██████████

Petitioner,

v

File No. 148219-001

Blue Cross Blue Shield of Michigan,

Respondent.

Issued and entered
this 12th day of June 2015
by Randall S. Gregg
Special Deputy Director

ORDER

I. BACKGROUND

██████████ (Petitioner) receives health care benefits through a group plan that is underwritten by Blue Cross Blue Shield of Michigan Mutual Insurance Company (BCBSM).

The Petitioner was diagnosed with “metastatic appendiceal carcinoma with peritoneal carcinomatosis” in December 2013. According to his physician, he has exhausted all standard treatments that he was able to tolerate. When the Petitioner’s physician asked BCBSM to cover the prescription drug Mekinist (trametinib) to treat his cancer, BCBSM denied the request.

The Petitioner appealed BCBSM’s denial through an expedited internal appeal. At the conclusion of that process, BCBSM issued a final adverse determination dated May 6, 2015, upholding its denial on the basis that the Petitioner did not meet its criteria for coverage of Mekinist.

On June 9, 2015, ██████████ the Petitioner’s authorized representative, filed a request with the Director of Insurance and Financial Services for an expedited external review of BCBSM’s final adverse determination under the Patient’s Right to Independent Review Act, MCL 550.1901 *et seq.* The Director accepted the request on June 10, 2015.

Because medical issues are involved the Director assigned the matter to an independent medical review organization which provided its analysis and recommendation on June 11, 2015.

II. ISSUE

Did BCBSM correctly deny coverage for Mekinist?

III. ANALYSIS

BCBSM's Argument

In its final adverse determination, BCBSM explained to the Petitioner its reason for denying coverage:

This letter is regarding an expedited appeal that was submitted on your behalf . . . regarding the authorization denial of the prescription drug Mekinist (trametinib). After clinical pharmacist review, the authorization denial is maintained. The criteria required for approval are not met.

* * *

The *BCBSM/BCN Custom Drug List (January 2015)* identifies that Mekinist requires prior approval on Page 46 of the drug list.

* * *

As indicated on Page 34 of the *Blue Cross Blue Shield of Michigan (April 2015) Prior Authorization and Step Therapy Guidelines*, Mekinist requires prior approval/step therapy as follows:

Mekinist – Coverage will be provided for the treatment of advanced and metastatic melanoma in patients who have BRAF V600E or V600K mutations.

* * *

A Clinical Pharmacist, R.Ph. reviewed the documentation provided by the office of [your physician] regarding the authorization denial of the prescription drug Mekinist (trametinib). Based on our review, the following was determined:

The coverage guidelines for your Custom Drug List benefit require criteria be met before coverage can be authorized. Our criteria for coverage of this medication requires documentation (chart notes) of a diagnosis of unresectable or metastatic melanoma with BRAF V600E or V600K mutation as detected by an FDA-approved test. We have no record (chart notes) of this diagnosis. Please see National Comprehensive Cancer Network (NCCN) recommendations and pathways for potential treatment options. Consideration for coverage may be given for NCCN recommended therapies.

As a point of clarification, Mekinist (trametinib) is covered under your prescription drug benefit; however, clinical criteria must be met for prior authorization. Because we do not have the supporting documentation (chart notes) to identify the diagnoses required for approval, the authorization denial is maintained.

Petitioner's Argument

In a letter dated May 29, 2015 submitted for this external review, the Petitioner's oncologist wrote:

[The Petitioner] was originally diagnosed with metastatic appendiceal carcinoma with peritoneal carcinomatosis in December 2013. He was treated with four cycles of FOLFOX at which point progression by CT scan and markers was found. In March 2014 he underwent debulking which included a partial resection of R diaphragm, LUQ peritonectomy, pelvic peritonectomy, re-colectomy, splenectomy, cholecystectomy, and then HiPEC with mitomycin. Imaging in April 2014 showed minimal residual disease; however, biopsy of peritoneum in May 2014 showed new adenocarcinoma. This patient was observed until July 2014 at which time FOLFIRI with bevacizumab was started and continued through November 2014. He was subsequently admitted to the hospital with diarrhea and dehydration. [His] therapy was changed to bevacizumab and capecitabine in January 2015, requiring capecitabine dose reduction due to toxicities. In March 2015, FOLFIRI and bevacizumab were resumed due to increasing markers and inability for patient to tolerate higher capecitabine doses. FOLFIRI and bevacizumab were stopped after two cycles due to recurrent bowel obstruction and intolerable symptoms. Presently, [the Petitioner] is planned for HiPEC with melphalan followed by trametinib.

All standard treatments have been exhausted with this patient to the extent that he was able to tolerate these therapies. Although it has been noted that this medication is not covered for [the Petitioner's] particular diagnosis and genetic mutations, it is a well-tolerated oral therapy that has been used in similar patients with SMAD4 mutation with favorable results. [He] has documented expression of the GNAS, KRAS and SMAD4 mutation. All three of these mutations have been shown to be associated with appendiceal carcinoma. Trametinib was used in similar patients with SMAD4 mutation and discussed at a recent symposium. GNAS mutations, in particular, have been shown to activate the Wnt and ERK 1/2 MAPK pathways leading to tumorigenesis and in the development of pancreatic cysts. MAPK Inhibition, in turn, has been shown to reduce mucinous tumor growth in appendiceal carcinomas. As MEK lies downstream within this pathway it logically follows that a MEK inhibitor would be the next step. {Citations omitted}

Director's Review

The Petitioner's drug benefits are defined in BCBSM's *Preferred Rx Program Certificate LG*¹ (the certificate). Some drugs require that certain criteria be met before they are authorized for coverage. BCBSM applied its criteria when it reviewed the Petitioner's request for Mekinist.

In an external review under the Patient's Right to Independent Review Act (PRIRA), when the issue involves a review of medical necessity or clinical review criteria, the Director assigns the case to an independent review organization (IRO) for analysis and a recommendation as required by section 11(6) of PRIRA, MCL 550.1911(6).

The IRO physician reviewer is board certified in internal medicine, medical oncology, and hematology, has been in practice for more than 12 years, and is familiar with the medical management of

¹ BCBSM form no. 834E, effective 2015.

patients with the Petitioner's condition. The IRO report included the following analysis and recommendation:

The results of the consultant's review indicate that this case involves a 45 year-old male who has a history of appendiceal carcinoma with peritoneal carcinomatosis. At issue in this appeal is the request for authorization and coverage for Mekinist (trametinib) for treatment of the member's condition.

The member has received FOLFOX for 4 cycles, but his tumor progressed. In March 2014, the member had extensive debulking surgery with hyperthermic peritoneal chemotherapy with mitomycin. There were biopsy-proven signs of progression by May 2014. The member was observed until July 2014, when he received FOLFIRI/bevacizumab until November 2014, when he developed toxicities to the irinotecan including diarrhea and volume depletion requiring hospitalization. In January 2015, the member had a capecitabine dose reduction. By March 2015, FOLFIRI/bevacizumab were resumed and capecitabine was discontinued. The regimen was stopped with the member developed bowel obstruction and additional toxicities. The member was evaluated in April 2015 by his oncologist, who recommended trametinib therapy as a reasonable next step.

Patients with refractory or relapsed cancer who have exhausted standard treatments are usually considered for clinical trials. It has recently become important to identify mutations that may be amenable to targeted therapy. A study of 86 patients in which progression-free survival on a regimen selected by molecular profile was compared to progression-free survival on the last chemotherapy regimen found that the regimen selected by molecular profiling offered a 27% survival advantage.

Mekinist is a new inhibitor of MEK kinases approved for use in metastatic melanoma with mutant BRAF. The Health Plan's criteria provide coverage of Mekinist for treatment of advanced and metastatic melanoma in patients who have BRAF V600E or V600K mutations. However, the MAXIMUS physician consultant explained that the MEK kinases are within the same pathway as RAF and BRAF. The physician consultant also explained that thus, it is mechanistically appealing to apply trametinib to tumors with constitutive RAS signaling, such as this member's tumor. A phase I trial showed that trametinib was tolerated at 2 milligram twice a daily with some responses in patients with colon cancer. A plenary paper presented at the American Society of Clinical Oncology showed one complete response and some partial responses with trametinib and dabrafenib in patients with BRAF mutant colon cancer. The physician consultant explained that this member would be offered off-label treatment or participation in a phase I or II clinical trial, but the results of the molecular profiling offer a rational selection of the next regimen. The consultant indicated that treatment with this FDA approved drug is medically necessary for the member. The physician consultant also indicated that the member meets criteria A through E of the Michigan statute included with the case assignment [*i.e.*, MCL 500.3406e, *antineoplastic drugs*].

Pursuant to the information set forth above and available documentation, the MAXIMUS physician consultant determined that Mekinist is medically necessary for treatment of the member's condition. [Citations omitted]

The Director is not required to accept the IRO's recommendation. *Ross v Blue Care Network of Michigan*, 480 Mich 153 (2008). However, the recommendation is afforded deference by the Director. In a decision to uphold or reverse an adverse determination, the Director must cite "the principal reason or reasons why the [Director] did not follow the assigned independent review organization's recommendation." MCL 550.1911 (16)(b).

The IRO's analysis is based on experience, expertise, and professional judgment. The Director, discerning no reason why the IRO's recommendation should be rejected in the present case, finds that Mekinist is medically necessary to treat the Petitioner's condition.

IV. ORDER

The Director reverses BCBSM's May 6, 2015, final adverse determination. BCBSM shall immediately cover Mekinist for the Petitioner's treatment, and shall, within seven days of providing coverage, furnish the Director with proof it has implemented this order.

To enforce this order, the Petitioner may report any complaint to the Department of Insurance and Financial Services, Health Care Appeals Section, at this toll free telephone number: (877) 999-6442.

This is a final decision of an administrative agency. Under MCL 550.1915, any person aggrieved by this order may seek judicial review no later than 60 days from the date of this order in the circuit court for the county where the covered person resides or in the circuit court of Ingham County. A copy of the petition for judicial review should be sent to the Department of Insurance and Financial Services, Office of General Counsel, Post Office Box 30220, Lansing, MI 48909-7720.

Patrick M. McPharlin
Director

For the Director:



Randall S. Gregg
Special Deputy Director